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USSN: CPA of 09/464,795

#16  
Dice  
6/18/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Contag and Zhang

Serial No.: CPA of 09/464,795

Art Unit: 1632

Filing Date: 16 December 1999

Examiner: R. Shukla

Title: NON-INVASIVE EVALUATION OF PHYSIOLOGICAL RESPONSE IN A  
MAMMAL

DECLARATION OF DAVID B. WEST, PhD  
PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

I, David B. West, hereby declare as follows:

1. I received my Bachelors of Science Degree in Biology from the University of Washington in 1977; and my Doctorate of Philosophy Degree in Physiology and Psychology in 1984 from the University of Washington.
2. I am currently the Senior Director of Preclinical Reserach at Xenogen Corporation and have held this position since April 9, 2001. Before joining Xenogen, I worked as Director of Mouse Genetics at Pfizer, Incorporated. Additional details regarding my background and qualifications can be found in the accompanying copy of my *Curriculum Vitae*.
3. I have reviewed pending Patent Application Serial No. 09/464,795 for "NON-INVASIVE EVALUATION OF PHYSIOLOGICAL RESPONSE IN A MAMMAL " by Contag and Zhang, (hereinafter "the specification") including pending claims 38, 40, 41, 43, 45, 46, 49 and 65-68. I have also reviewed (1) the Final Office Action dated September 13, 2001; (2) Cameron (1997) *Molecular Biotechnology* 7:253-

Considered  
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265; and (3) Cui et al. (1994) *Transgenic Research* 3:182-194. Therefore, I am familiar with the issues raised by the Examiner.

4. I understand that pending claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are directed to transgenic mice and methods of using such mice. In particular, I understand that the transgenic mice comprise a panel of expression cassettes. Each expression cassette of this panel includes a control element from a stress-inducible gene operably linked to a sequence encoding a light-generating protein. Similarly, I understand that there are methods of using such mice to determine the effect of an analyte on gene expression.

5. In December of 1999, when the specification was filed, a typical scientist working the field of transgenic animals had a Ph.D. in the Biological or Chemical Sciences and two to five years of relevant experience. I will call such a person a "typical scientist."

6. When the specification was filed, it clearly conveyed to a typical scientist that the inventors had in their possession the invention of the claims (as set forth in paragraph 4, above). By "in their possession," I mean that the inventors contemplated transgenic mice comprising a panel of expression cassettes, wherein the panel comprises at least two different expression cassettes, each having a different stress-inducible control element operably linked to sequence encoding a light-generating polypeptide, and that they had, using the specification and information available to a typical scientist, a practical way of making and using such transgenic mice. Thus, I believe that a typical scientist would have understood the specification clearly described all of the various aspects of the claims and enabled a typical scientist to make and use the invention as set forth in the pending claims. I base this belief on the facts set forth below.

7. First, at the time the specification was filed, it was widely known how to construct expression cassettes generally. With regard to expression vectors comprising control elements from stress-inducible promoters operably linked to a sequence encoding a light-generating polypeptide, such methods are described in detail in the specification, for example, in Section 3.1.0 of the specification. Therefore, it is my opinion that construction of a panel of expression cassettes as set forth in the claims would have been routine to a typical scientist working in this area in view of the teachings of the specification.

8. Second, it would have been clear to a typical scientist that the inventors had in their possession the various polynucleotide components of the expression cassettes. Control elements derived from stress-inducible genes were known and clearly set forth in the specification at the time of filing. (See, Section 3.1.1 starting on page 35

of the specification). Similarly, the specification clearly describes sequences encoding light-generating proteins. (See, Section 3.2.0 starting on page 58 of the specification). Thus, it is my opinion that light-generating polypeptide-encoding sequences operably linked to control elements derived from stress-inducible genes of the expression cassettes of the claims are fully described in the specification.

9. Third, it would have been plain to a typical scientist from the specification that the inventors were in possession of an operative way of making the claimed transgenic mice. The specification describes methods of making transgenic animals on page 59, line 28 to page 60, line 8 and in the references cited therein. At the time the application was originally filed, such methods were routine to the typical scientist. Indeed, methods of introducing multiple expression constructs, each with their own separate promoter, to create transgenic founders are described in the art. (See, *e.g.*, Jankowsky et al. (2001) *Biomol Eng* 17(6):157-165, copy of the Abstract attached hereto). Also routine at the time of filing were methods of assaying if a sequence from an expression cassette had been integrated into a host mouse's genome and, if so, where such integration occurred. Such assay methods include, but are not limited to, PCR, Northern and/or Southern blotting (for example of particular tissues) as well as *in situ* hybridization and/or imaging techniques.

10. Fourth, a typical scientist would have known that the inventors were in possession of operative methods of using these transgenic mice, for example, to determine the effect of an analyte. The evaluation of whole transgenic animals having light-reporter systems is described on line 29, page 60 through line 6, page 61 of the specification. It is also my opinion that applying these methods of evaluation to the claimed transgenic mice and methods of using these mice would have been routine to one working in this area in view of Applicants teachings.

11. It is further my opinion that one skilled in the art would understand from the specification that the claimed transgenic mice could be made using techniques described in the specification or known at the time of filing. (See, *e.g.*, page 59, line 28 to page 60, line 8). Further, the specification discusses how to prepare transgenic animals and how to performing imaging experiments on these animals, etc. Thus, I believe that, based on the application and level of skill in the art, one working in this field would be able to make and use the claimed transgenic mice.

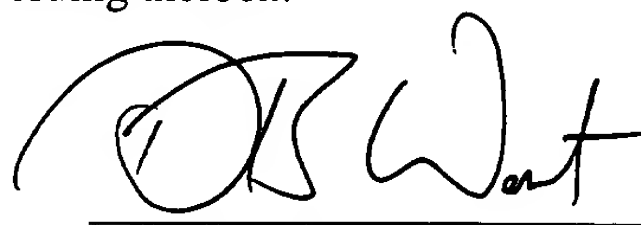
12. It is further my opinion that Cameron and Cui are not relevant to the subject matter claimed in the application. Cameron is directed primarily to transgenic livestock. (See, Cameron, Abstract). Further, the issues raised in Cameron regarding poor levels of expression are not relevant to the claimed invention for a variety of

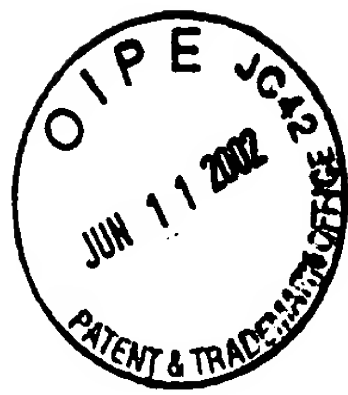
reasons. First, transgenic mice containing the claimed expression cassettes can be readily assayed for expression levels and only those animals exhibiting the desired expression levels can be used. (See, also, paragraph 9 above). Second, leaky expression is not a major issue in the practice of the present invention -- where the expression cassettes integrate is irrelevant so long as expression of the light-generating protein is inducible via a stress-inducible control element. (See, also, paragraph 9 above). For its part, Cui is not relevant to the claimed invention because it is not directed to the use of light-generating proteins as *in situ* reporters. (See, Cui, page 183). Thus, I believe that one working in this field would have no reason to apply this information to the claimed invention. Accordingly, I do not believe that Cameron or Cui to be relevant to the claimed invention.

13. Therefore, taken as whole, the specification unambiguously conveyed to a typical scientist that the inventors contemplated including a panel of expression cassettes in a transgenic mouse comprising the stress-inducible control element operably linked to light-generating polypeptide-encoding sequence as disclosed in the specification. The inventors also had in their possession an operative way of using these transgenic animals to evaluate the effect of analyte in a whole animal. In sum, based on the disclosure of the specification and the level of knowledge of a typical scientist regarding expression cassettes, transgenic animals and assays for integration available at the time of filing, I believe that the specification as filed clearly conveys that the applicants had invented the expression cassettes and methods as set forth in the claims.

14. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

May 8 2002  
Date

  
David B. West, Ph.D.



## CURRICULUM VITAE

**David B. West, Ph.D.**

### PERSONAL

Place of Birth: Pittsburgh, PA  
Citizenship: United States  
SSN: 536-56-5817

Sr. Director of Preclinical Research  
Xenogen Corporation  
860 Atlantic Avenue  
Alameda, CA 94501  
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FAX: 510-291-6136  
E-MAIL: david.west@xenogen.com

Visiting Scientist  
Lawrence Berkeley National Laboratory  
Berkeley, CA

Home Address:

5840 St. Paul Court  
Oakland, CA 94618  
TEL: 510-339-2912

### EDUCATION

1983                      Ph.D. in Physiology/Psychology  
                             University of Washington, Seattle, WA  
                             Dissertation Title: Abnormal Perinatal and Infant  
                             Nutrition as a Cause of Obesity: Development of an  
                             Animal Model

1976                      B.S. Cellular and Molecular Biology,  
                             Cum Laude and Phi Beta Kappa  
                             University of Washington, Seattle, WA

## **PROFESSIONAL EXPERIENCE**

- |                       |  |
|-----------------------|--|
| April 2001 – Present  | Sr. Director of Preclinical Research<br>Xenogen Corporation<br>Alameda, CA   |
| June 2000 – Jan. 2001 | Director of Mouse Genetics<br>Pfizer Global Research and Development<br>Alameda, CA  |
| May 1998 – June 2000  | Director of Mouse Genetics<br>Parke-Davis Laboratory for Molecular Genetics<br>Alameda, CA   |
| June 1999 – Present   | Visiting Scientist<br>Lawrence Berkeley National Laboratory<br>Department of Molecular Medicine  |
| May 1998 - Present    | Adjunct Professor<br>Pennington Biomedical Research Center   |
| Mar. 1997 - Mar. 1998 | On 75% time Academic Leave<br>Participated in start-up of gene/Networks, Inc.<br>A biotechnology company.  |
| Sept. 1996 - 1998     | Professor, Pennington Biomedical Research Center and<br>Adjunct Professor in School of Veterinary Medicine and<br>School of Medicine, Louisiana State University |
| Feb. 1991 - 1996      | Associate Professor<br>Pennington Biomedical Research Center<br>Louisiana State University   |
|                       | Adjunct Associate Professor<br>Department of Physiology<br>School of Veterinary Medicine<br>Louisiana State University   |
|                       | Adjunct Associate Professor<br>Department of Physiology<br>Louisiana State University<br>School of Medicine<br>New Orleans, LA<br>(Effective 1993)               |

1987 - Feb. 1991	Assistant Professor of Physiology and Internal Medicine Eastern Virginia Medical School Norfolk, VA Staff Scientist Veterans Administration Medical Center Hampton, VA
1986 - 1987	Adjunct Assistant Professor of Biology Vassar College Poughkeepsie, NY
1984 - 1986	Individual NIH Postdoctoral Fellow Sponsor: Greenwood, M.R.C. Vassar College Poughkeepsie, NY
1977 - 1983	NIH Predoctoral Fellow in the Departments of Physiology and Psychology University of Washington Seattle, WA

### **RELATED PROFESSIONAL EXPERIENCE**

1984 - 1987	Writer, Medical Literature Review Corporation St. James, NY
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### **RESEARCH FUNDING**

March, 1998- February, 2002	National Institutes of Health RO1 #DK53393 An obesity locus on mouse chromosome 7 Estimated total direct costs for 4 years: \$1,002,628 Approximately 40% of project subcontracted to Dr. Dabney Johnson, Oakridge National Laboratory
1994 - Sept, 2001	National Institutes of Health RO1 #DK45895 Metabolic and genetic markers for dietary obesity Current funding period September 1, 1997 - August 31, 2001 Estimated total direct costs for 4 years: \$1,160,521
Jan, 1998 - Dec, 1999	National Cattleman's Beef Association Co-PI with James P. DeLany Effects of conjugated linoleic acid on metabolism in the mouse.

Estimated total direct costs for 1 year: \$75,000

- |             |   |
|-------------|---|
| 1991 - 1996 | National Institutes of Health R29 #DK44446<br>Nutrition and hypertension: Role of hyperinsulinemia  |
| 1991 - 1992 | Pew National Nutrition Program<br>Fellowship for Faculty Scholars in Nutrition  |
| 1989 - 1990 | Diabetes Center of Eastern Virginia<br>Grant in Aid.<br>Insulin resistance and dietary obesity: Role of<br>altered renal function in the development of<br>obesity-related hypertension |
| 1987 - 1988 | Eastern Virginia Medical School<br>Institutional Research Grant<br>Obesity and Hypertension   |
| 1985 - 1988 | National Institutes of Health ROI #HD12637<br>Co-Principal Investigator with Greenwood, M.R.C.,<br>Nutrition and adipocyte growth and<br>development                                    |
| 1985 - 1987 | Hoffmann-La Roche Inc.<br>Research Contract<br>Peptides and feeding behavior  |
| 1985 - 1987 | New York Heart Association<br>Grant-in-Aid<br>Co-Principal Investigator with Greenwood, M.R.C.,<br>Altered blood flow and metabolism in obese<br>fa/fa rats                             |
| 1984 - 1986 | National Institutes of Health<br>Individual Postdoctoral Fellowship #AMO7332<br>Early nutritional factors in the etiology of obesity  |

### **RESEARCH INTERESTS**

Molecular genetics of obesity  
Molecular genetics of complex disorders  
Obesity and hypertension  
Early nutrition in the etiology of obesity  
Adipose tissue physiology and metabolism



### **ACADEMIC RESEARCH IN PROGRESS**

NIH-funded:      Genetic and metabolic basis of dietary obesity  
                         Cloning an obesity gene on mouse chromosome 7

Other:              Metabolic effects of conjugated linoleic acid

### **TEACHING EXPERIENCE**

1987 - 1991      Eastern Virginia Medical School:  
                         Physiology: Year 1 Medical Students

1984 - 1987      Vassar College:  
                         Guest Lecturer, Endocrinology  
  
                         Laboratory Instructor in Nutrition (Supervisor of a minimum of 3  
                         independent students each year)  
                         Guest Lecturer, Principles of Nutrition

1982              University of Washington:  
                         Instructor, Surgical and Histological Techniques

1981              Teaching Assistant, Animal Learning Laboratory

1978 - 1980      Teaching Assistant, Surgical and Histological Techniques

### **TEACHING INTERESTS**

Molecular Genetics  
Nutrition  
Physiology  
Metabolism and Endocrinology

### **GRADUATE STUDENTS SUPERVISED**

Gerald Thompson, Department of Kinesiology, Louisiana State University; Ph.D. awarded in July, 1996.  
Dissertation: Post-exercise Hypotension in the Dog

Agatha Borne, DVM, Department of Physiology, School of Veterinary Medicine, Louisiana State University; Ph.D. awarded in May, 1998.

Dissertation: Interaction of Nitric Oxide and the Sympathetic Nervous System in the Control of Regional Vascular Resistance

### **MEMBERSHIPS IN SCIENTIFIC AND ACADEMIC SOCIETIES**

American Association for the Advancement of Science

American Institute of Nutrition

American Physiological Society

North American Association for the Study of Obesity

Society for the Study of Ingestive Behavior

### **ACADEMIC HONORS AND AWARDS**

1984 - 1986      NIH Individual Postdoctoral Fellowship  
Vassar College, Poughkeepsie, NY

1981              NSF Undergraduate Research Program Grant Co-  
sponsor with Stephen C. Woods, Ph.D.  
University of Washington, Seattle, WA

1980 - 1981      Graduate School Research Fund Grant  
Recipient (co-authored with Herman Samson, Ph.D.)  
Mechanisms of Satiety Hormones  
University of Washington, Seattle, WA

1977 - 1982      NIH Predoctoral Fellow  
University of Washington, Seattle, WA

1976              Bachelor of Science  
University of Washington, Seattle, WA  
Cum Laude and Phi Beta Kappa

### **NATIONAL PROFESSIONAL SERVICE**

1997              Ad hoc member, NIH Special Study Section

1996              Ad hoc member, NIH Special Study Sections

Organizing Committee, 1998 Summer FASEB Conference on  
Behavioral and Metabolic Subphenotypes in Obesity

1995                      Organizing Committee, Annual Meeting for the North  
American Association for the Study of Obesity

Ad hoc member, NIH Special Study Section

1994 - 1996            Education Committee, North American Association for  
the Study of Obesity

1993:                    Ad hoc member Nutrition Study Section  
CNRU Site Visit Team, National Cancer Institute

### **INSTITUTIONAL SERVICE**

1993 - 1997            Institutional Animal Care and Use Committee  
Pennington Biomedical Research Center

1990 - 1991            Chairman, Curriculum Committee  
Eastern Virginia Medical School

1989 - 1990            Member, Curriculum Committee  
Eastern Virginia Medical School

1988 - 1991            Institutional Animal Care and Use Committee  
Veterans Affairs Medical Center, Hampton, VA

### **AD HOC REVIEWER**

American Journal of Physiology  
Appetite  
Genomics  
International Journal of Obesity  
Journal of Nutrition  
Journal of Clinical Nutrition  
Journal of Clinical Investigation  
Mammalian Genome  
Metabolism  
Obesity Research  
Peptides  
Physiology & Behavior

Proceedings of the National Academy of Science

### **EDITORIAL BOARDS**

American Journal of Physiology (1993)

### **INVITED PRESENTATIONS**

- 2000: "Mouse Models and Functional Genomics". Invited speaker at the Jackson Laboratory/Roche Laboratory symposium on Functional Genomics of Diabetes And Obesity. Palo Alto, CA.
- 1999: "Complex Genetics of Obesity". Invited speaker at 1999 Neuroscience Festival at the University of Cincinnati, Cincinnati, OH
- Panelist: "Dietary fat and obesity" 1999 meeting of the Society for Experimental Biology, Washington D.C.
- "Congenic Lines and the Deconvolution of Complex Genetics". Invited seminar speaker at the University of Oregon Health Sciences Center, Department of Neurosciences, Portland, OR
- "Mouse Genetics/Genomics for Target Identification and Validation". Invited Speaker at the annual winter conference on Medicinal and Bio-organic Chemistry, Park City, UT
- 1998: "Genetic Basis of High-Fat Induced Obesity". Presentation at the 8<sup>th</sup> International Congress on Obesity, Paris, France
- "Obesity QTLs in Rodents". American College of Sports Medicine. Symposium on Obesity, Orlando, FL
- "Man-Mouse Synteny: A Paradigm for Unraveling the Complexity of Human Genetic Disorders". March of Dimes Symposium on Complex Human Genetic Disorders. Los Angeles, CA
- "Dietary Fat and Gene Interactions". Pennington Biomedical Research Center Symposium on "Nutrition, Genetics and Obesity", Baton Rouge, LA
- 1997: "Genetics of Obesity in Animal Models: Relevance to Obesity Associated Hypertension. Presented at 1997 Experimental Biology

Symposium on Obesity and Hypertension. New Orleans, LA

1996: "Genetics and Physiology of Dietary Obesity in the Mouse" presented to:  
Department of Clinical Nutrition, University of Texas Southwestern  
Medical School, Dallas TX

Smith Kline Beecham, Welwyn Garden City, England

School of Agriculture, University of Nebraska, Lincoln NB

Symposium on Genetics of Obesity in Animal Models,  
Experimental Biology 1996 Annual Meeting, Washington, D.C.

2nd International Conference on Oils and Disease, University of  
Texas Southwestern Medical School, Dallas TX

Sixth Benjamin Franklin Lafayette Seminar on Mechanisms of  
Food Intake and Specific Appetites, Sponsored by Cornell University,  
Pennsylvania State University, and College de France,  
La Napoule, France

Third International Symposium on Obesity and NIDDM, Sponsored by  
The Clore Laboratory at the University of Buckingham, Buckingham  
England

Department of Nutritional Sciences, University of Illinois, Champagne-  
Urbana, IL

Biology Section, Oakridge National Laboratory, Oakridge, TN

Psychology Department, Florida State University, Tallahassee FL

1995: FASEB Summer Research Conference on Genetic and  
Behavioral Influences on Nutrient Metabolism and  
Obesity, Copper Mountain, CO. "Molecular Genetics  
of Dietary Obesity in the Mouse"

NIH, NIDDK Conference on Prevention and Treatment  
of Childhood Obesity, Bethesda, MD. "Molecular  
Genetics: Implications for Pediatric Obesity Research"

Annual Meeting of the North American Association  
for the Study of Obesity, Baton Rouge, LA. "Dietary  
Fat and Obesity: Genetic Models of Obesity in Animals"

CME Course on the Prevention and Treatment of  
Obesity in Special Populations, New Orleans, LA.  
"Genetics/Environment is the Primary Determinant  
of Most Cases of Obesity"

1994: Symposium on the Molecular and Genetic Aspects of  
Obesity, Pennington Biomedical Research Center  
Baton Rouge, Louisiana "Genetics of Dietary Obesity"

Seventh International Congress on Obesity  
Toronto, Canada  
Round Table Discussant; Prevention of Obesity

Obesity, Diabetes, and Insulin Resistance:  
Implications from Molecular Biology, Epidemiology,  
and Experimental Studies in Humans and Animals  
American Diabetes Association  
Boston, Massachusetts  
"Dietary Obesity, Insulin Resistance, and Hypertension, A Canine Model"

Visiting Scientist, Jackson Laboratory,  
Bar Harbor, Maine "Molecular Genetics of Dietary  
Obesity in the Mouse"

1993: Division of Cardiology  
Obesity Training Grant Speakers Program  
University of California  
Los Angeles, California  
"Genetics of Dietary Obesity in the Mouse"

Department of Nutrition  
University of California  
Davis, California  
"Genetics of Dietary Obesity in the Mouse"

First Department of Internal Medicine  
Gunma University School of Medicine  
Gunma, Japan

"Genetics and Physiology of Dietary Obesity in the Mouse"

- 1992: Continuing Medical Education  
Emory University  
Obesity Update: Pathophysiology, Clinical Consequences, and Therapeutic Options  
"Hypertension and Obesity"
- 1991: Fifth Benjamin Franklin/Lafayette Symposium on the Physiology of Appetitive Behavior  
La NaPoule, France  
"Dietary Obesity in Mice"
- 1989: FASEB Summer Research Conference on Energy Metabolism.  
Saxtons River, VT  
"Adipose Tissue Blood Flow and Metabolism"
- Annual meeting of the North American Association for the Study of Obesity  
Washington, DC  
"Animal Models of Obesity Associated Hypertension"
- 1988: Benjamin Franklin/Lafayette Symposium on the Physiology of Appetitive Behavior  
La NaPoule, France  
"Peptide Hormones and the Control of Food Intake"
- Buckingham University  
Symposium on Insulin and Obesity  
Buckingham, England  
"Regulation of Adipose Tissue Blood Flow by Insulin"
- 1987: Appetitive Seminar  
Columbia University, New York, NY  
"The Use of Short-acting Anorectic Agents for the Long-term Reduction of Food Intake"
- Fifth Annual Virginia Nutrition Conference  
"Role of Genetics and Adipocyte Development"

Harvard Medical School Continuing Education  
Program on Treatment of Obesity: Diet,  
Pharmacology, and Surgical Approaches  
Cambridge, MA  
"Cholecystokinin and Other Peptide Hormones"

1986: Department of Pharmacology  
Hoffman La-Roche, Nutley, NJ  
"Peptides and the Chronic Suppression of Food  
Intake"

Department of Psychology  
State University of New York, Albany, NY  
"Early Nutrition and the Development of Obesity"

Department of Nutrition  
University of Georgia, Athens, GA  
"Experimental Approaches in Animals to Study the  
Causes and Consequences of Obesity"

## **REFERENCES**

Ron Krauss, M.D.  
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University of California  
Donner Laboratory, Room 459  
One Cyclotron Road  
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## **PUBLICATIONS**

Iakoubova, O.A., Olsson, C.L., Dains, K.M., Choi, J., Kalcheva, I., Bentley, L.G., Cunanan, M., Hillman, D., Louie, J., Machrus, M. and West, D.B. Microsatellite marker panels for use in high-throughput genotyping of mouse crosses. In Press: *Physiological Genomics*.

Dhar M, LS Webb, L Smith, L Hauser, DKJohnson and DB West. A Heterozygous Deletion of a Novel ATPase Gene on Mouse Chromosome 7 Increases Body Fat. In Press: *Physiological Genomics*.

West DB, Y Ma, AA Truett, B York. Identification of Genes Involved in Animal Models of Obesity. *Handbook of Experimental Pharmacology: Obesity Pathology and Therapy*, Volume 149. D.H. Lockwood & T.G. Heffner (eds), Springer-Verlag, New York, pp 427-459, 2000.

West DB, FY Blohm, AA Truett, JP DeLany. Conjugated linoleic acid persistently increases total energy expenditure in AKR/J mice with no significant increase in uncoupling protein gene expression. *J Nutr*. 130(10): 2471-7, 2000.

Congenic Strains Confirm An Obesity Locus On Mouse Chromosome 4 Which Displays Regional Specificity and Epistatic Interactions. David B. West, James M. Cheverud, Alycia A. Truett, Tom Borges, Gary Truett and Barbara York Accepted with revisions by *Mammalian Genome*

Smith BK, PK Andrews and DB West. Macronutrient diet selection in thirteen mouse strains. *Am J. Physiol*. 278: R797-R805, 2000.

West DB, O Iakoubova, C Olsson, D Ross, J Ohmen & A Chatterjee. Mouse Genetics/Genomics: An effective approach for drug target discovery and validation. In *Medicinal Research Reviews* 20(3): 216-230, 2000.

York, B., and West, D.B. Polygenic models of rodent obesity. *Pennington Center Nutrition Series: Volume 9*. G.A. Bray & D.H. Ryan (Eds), Louisiana State University Press, Baton Rouge, pp 46-72, 1999.

Smith BK, PK Andrews, DA York, DB West. Divergence in proportional fat intake in AKR/J and SWR/J mice endures across diet paradigms. *Am. J. Physiol*. 277: R776-785, 1999.

York B, AA Truett, MP Monteiro, SJ Barry, CH Warden, JK Naggert, TP Maddatu, DB West. Gene-environment interaction: a significant diet-dependent obesity locus demonstrated in a congenic segment on mouse chromosome 7. *Mammalian Genome* 10: 457-462, 1999.

Delany JP, F Blohm, AA Truett, JA Scimeca, DB West. Conjugated linoleic acid rapidly reduced body fat content in mice without affecting energy intake. *Am. J. Physiol*. 276: R1172-R1179, 1999.

West DB & B York. Molecular genetics of dietary obesity in the mouse. In: *Progress in Obesity Research*, pp 145-149. J. Libbey and Company Ltd. London and New York, B Guy-Grand and G Ailhaud, eds. 1999.

Geiselman, P.J., Anderson, A.M., Dowdy, M.L., West, D.B., Redmann, S.M., and Smith, S.R. Reliability and validity of a macronutrient self-selection paradigm and a food preference questionnaire. *Physiology and Behavior*. 63: 919-928, 1998.

- West, D.B., DeLany, J.P., Camet, P.M., Blohm, F., Truett, A.A., and Scimeca J. Effects of Conjugated linoleic acid on body fat and energy metabolism in the mouse. *Am J Physiol* 275: R667-R672, 1998.
- West, D.B., and York, B. Dietary fat, genetic predisposition, and obesity: lessons from animal models. *Am J Clin Nutr* 67(Suppl 3): 505S-512S, 1998.
- West, D.B., and York, B. Mouse models of human overweight. In: *Human Polygenic Diseases*, Dragani, T.A., Ed., Harwood Academic Publishers, pp 113-129, 1998
- Truett A.A., Borne, A.T., Monteiro, M.P., and West, D.B. Composition of dietary fat affects blood pressure and insulin responses to dietary obesity in the dog. *Obesity Research* 6: 137-146, 1998.
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[Related Articles, Books, LinkOut](#)**Co-expression of multiple transgenes in mouse CNS: a comparison of strategies.****Jankowsky JL, Slunt HH, Ratovitski T, Jenkins NA, Copeland NG, Borchelt DR.**

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The introduction of two transgenes into one animal is increasingly common as transgenic experiments become more sophisticated. In this study we examine two strategies for creating double transgenic founders from a single microinjection. In the first approach, two constructs, each with its own promoter element, were coinjected into the pronucleus. In the second approach, both transgenes were cloned into one vector, separated by an internal ribosomal entry site (IRES), and placed under control of a single promoter. Both strategies save time and increase the percentage of double transgenic offspring over the standard method of mating single transgenic lines. However, despite high transgene copy numbers, the bicistronic lines did not show robust expression of either protein. Copy number and protein expression correlated much better in the coinjected lines, with expression levels in one line approaching that observed in some of our best single transgenic controls. Thus we recommend coinjection of individual plasmids for the generation of multiply transgenic founders.

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